

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

X 15050

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

17 SEP 2005

<p>Applicant's or agent's file reference see form PCT/ISA/220</p>		<p>Date of mailing (day/month/year) see form PCT/ISA/210 (second sheet)</p>	
<p>International application No. PCT/US2004/038226</p>	<p>International filing date (day/month/year) 06.12.2004</p>	<p>Priority date (day/month/year) 17.12.2003</p>	
<p>International Patent Classification (IPC) or both national classification and IPC C07C233/80, C07D213/75, A61K31/165, A61K31/44, A61P25/06</p>			
<p>Applicant ELI LILLY AND COMPANY</p>			

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

<p>Name and mailing address of the ISA.</p> <p> European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx. 31 651 epo nl Fax: +31 70 340 - 3016</p>	<p>Authorized Officer</p> <p>Fitz, W</p> <p>Telephone No +31 70 340-4359</p>
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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/038226

Box No. I Basis of the opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 a sequence listing
 table(s) related to the sequence listing
 - b. format of material:
 in written format
 in computer readable form
 - c. time of filing/furnishing:
 contained in the international application as filed.
 filed together with the international application in computer readable form.
 furnished subsequently to this Authority for the purposes of search.
3. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

the entire international application,
 claims Nos. 9-14 with respect to industrial applicability

because:

the said international application, or the said claims Nos. 9-14 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
 the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
 no international search report has been established for the whole application or for said claims Nos.
 the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

has not been furnished
 does not comply with the standard

the computer readable form

has not been furnished
 does not comply with the standard

the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes:	Claims	1-27
	No:	Claims	-
Inventive step (IS)	Yes:	Claims	1-27
	No:	Claims	-
Industrial applicability (IA)	Yes:	Claims	1-8,15-27
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 9-14 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following document:

D1: WO 98/55115 A

1.) The document D1 is regarded as being the closest prior art to the subject-matter of claim 1, and shows 5-HT1F agonists that are useful for the treatment of migraine.

The compounds proposed in present claim 1 differ from the known compounds of D1 in that they have a cyclohexenyl-phenyl core (whereas the compounds of D1 have a tetrahydrocarbazole core).

Accordingly, the subject-matter of claims 1-27 is new (Article 33(2) PCT).

2.) The problem to be solved by the present invention may be regarded as the provision of further 5-HT1F agonists for the treatment of migraine.

The solution to this problem proposed in claim 1 of the present application is considered as involving an inventive step (Article 33(3) PCT), because replacing a tricyclic carbazole moiety with the bicyclic cyclohexenyl-phenyl moiety of the present compounds is not an obvious measure. D1 alone, or in combination with another document of the prior art would not direct the skilled person towards compounds with a cyclohexenyl-phenyl core.

Accordingly, the subject-matter of claims 1-27 is considered as involving an inventive step (Article 33(3) PCT).

3.) For the assessment of the present claims 9-14 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

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patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

With respect to claims 1-8 and 15-27 there are no objections with respect to industrial applicability.

Re Item VIII

Certain observations on the international application

- 1.) The vague and imprecise statement in the description on page 5, lines 15-20 implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them.
- 2.) The expression "use according to claim 26" that is used in claim 25 appears to be erroneous with respect to the claim number, Article 6 PCT.